



Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children

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Table 2: Secondary Prophylaxis of Opportunistic Infections in HIV-Exposed and HIV-Infected Children—Summary of Recommendations (Last updated December 9, 2019; last reviewed December 9, 2019) (page 1 of 6)

Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Bacterial Infections <i>S. pneumoniae</i> and other invasive bacteria.	• TMP-SMX 75/375 mg/ m ² body surface area per dose by mouth twice daily	• IVIG 400 mg/ kg body weight every 2–4 weeks	<u>Secondary Prophylaxis Indicated:</u> • >2 serious bacterial infections in a 1-year period in children who are unable to take cART <u>Criteria for Discontinuing Secondary Prophylaxis:</u> • Sustained (≥ 3 months) immune reconstitution (CD4 percentage ≥25% if ≤6 years old; CD4 percentage ≥20% or CD4 count >350 cells/mm ³ if >6 years old) <u>Criteria For Restarting Secondary Prophylaxis:</u> • >2 serious bacterial infections in a 1-year period despite cART	November 6, 2013
Candidiasis	Not routinely recommended, but can be considered for frequent severe recurrences. <u>Fluconazole:</u> • Fluconazole 3–6 mg/ kg body weight daily (maximum 200 mg) by mouth, or itraconazole oral solution, 2.5 mg/kg body weight/dose twice daily	N/A	<u>Secondary Prophylaxis Indicated:</u> • Frequent or severe recurrences <u>Criteria for Discontinuing Secondary Prophylaxis:</u> • When CD4 count or percentage has risen to CDC immunologic Category 2 or 1 <u>Criteria for Restarting Secondary Prophylaxis:</u> • Frequent severe recurrences	January 31, 2019
Coccidioidomycosis	Fluconazole 6 mg/kg body weight (maximum 400 mg) by mouth once daily	Itraconazole 2–5 mg/kg body weight (maximum 200 mg) by mouth per dose twice daily	Lifelong secondary prophylaxis with fluconazole for patients with meningitis or disseminated disease in the immunocompromised patient is recommended. Secondary prophylaxis should be considered after treatment of milder disease if CD4 count remains <250 cells/mm ³ or CD4 percentage <15%.	November 6, 2013
Cryptococcosis^a	Fluconazole 6 mg/kg body weight (maximum 200 mg) by mouth once daily	Itraconazole oral solution 5 mg/ kg body weight (maximum 200 mg) by mouth once daily	<u>Secondary Prophylaxis Indicated:</u> • Documented disease <u>Criteria For Discontinuing Secondary Prophylaxis</u> <u>If All of the Following Criteria are Fulfilled:</u> • Age ≥6 years • Asymptomatic on ≥12 months of secondary prophylaxis • CD4 count ≥100 cells/mm ³ with undetectable HIV viral load on cART for >3 months <u>Criteria for Restarting Secondary Prophylaxis:</u> • CD4 count <100/mm ³ ^a Secondary prophylaxis is also referred to as maintenance therapy or suppressive therapy	November 6, 2013
Cryptosporidiosis	N/A	N/A	N/A	August 29, 2019

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Cytomegalovirus (CMV)	<ul style="list-style-type: none"> Ganciclovir 5 mg/kg body weight IV once daily, or For older children who can receive adult dose (based on their BSA), valganciclovir tablets 900 mg orally once daily with food, or For children age 4 months–16 years, valganciclovir oral solution 50 mg/mL (at dose in milligrams = $7 \times \text{BSA} \times \text{CrCl}$ up to maximum CrCl of 150 mL/min/1.73 m²) orally once daily with food, or Foscarnet 90–120 mg/kg body weight IV once daily 	<ul style="list-style-type: none"> Cidofovir 5 mg/kg body weight per dose IV every other week. Must be given with probenecid and IV hydration. 	<p><u>Secondary Prophylaxis Indicated For:</u></p> <ul style="list-style-type: none"> Prior disseminated disease, retinitis, neurologic disease, or GI disease with relapse <p><u>Criteria for Discontinuing Secondary Prophylaxis</u></p> <p><i>If All of the Following Criteria Are Fulfilled:</i></p> <ul style="list-style-type: none"> Completed ≥ 6 months of cART Consultation with ophthalmologist (if retinitis) Age <6 years with CD4 percentage $\geq 15\%$ for >6 consecutive months Age ≥ 6 years with CD4 cell count > 100 cells/mm³ for >6 consecutive months For retinitis, routine (i.e., every 3–6 months) ophthalmological follow-up is recommended for early detection of relapse or immune restoration uveitis. <p><u>Criteria for Restarting Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> Age <6 years with CD4 percentage $< 15\%$ Age ≥ 6 years with CD4 cell count < 100 cells/mm³ 	November 6, 2013
Giardiasis	N/A	N/A	N/A	August 22, 2019
Hepatitis B Virus (HBV)	Hepatitis A Vaccine	N/A	<p><u>Secondary Prophylaxis Indicated for:</u></p> <ul style="list-style-type: none"> Chronically HBV-infected individuals to prevent further liver injury <p><u>Criteria for Discontinuing Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> N/A <p><u>Criteria for Restarting Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> N/A 	November 6, 2013
Hepatitis C Virus (HCV)	None	N/A	N/A	November 6, 2013

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Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Herpes Simplex Virus (HSV) Infections	<p><u>Mucocutaneous Disease:</u></p> <ul style="list-style-type: none"> • Acyclovir 20 mg/kg body weight/dose (maximum 800 mg/dose) by mouth BID <p><u>Suppressive Therapy After Neonatal HSV Disease (Skin, Eye, Mouth, CNS, or Disseminated Disease):</u></p> <ul style="list-style-type: none"> • Acyclovir 300 mg/m² body surface area/dose by mouth TID for 6 months 	<p><u>Mucocutaneous Disease. For Adolescents Old Enough to Receive Adult Dosing:</u></p> <ul style="list-style-type: none"> • Valacyclovir 500 mg by mouth BID, or • Famciclovir 500 mg by mouth BID 	<p><u>Secondary Prophylaxis Indicated:</u></p> <ul style="list-style-type: none"> • Suppressive secondary prophylaxis can be considered for children with severe and recurrent mucocutaneous (oral or genital) disease <p><u>Criteria for Discontinuing Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> • After a prolonged period (e.g., 1 year) of prophylaxis, consider suspending prophylaxis and determine with the patient whether additional prophylaxis is necessary. Although level of immune reconstitution is a consideration, no specific CD4 threshold has been established. 	June 27, 2018
Histoplasmosis (Suppressive Therapy)	Itraconazole oral solution 5–10 mg/kg body weight (maximum 200 mg) per dose by mouth daily	Fluconazole 3–6 mg/kg body weight (maximum 200 mg) by mouth once daily	<p><u>Secondary Prophylaxis Indicated:</u></p> <ul style="list-style-type: none"> • Documented histoplasmosis in a patient with impaired immune function <p><u>Criteria For Discontinuing Secondary Prophylaxis</u></p> <p><i>If All of the Following Criteria Are Fulfilled:</i></p> <ul style="list-style-type: none"> • CD4 percentage >15% at any age; or CD4 cell count >150 cells/mm³ aged ≥6 years. • Received ≥1 year itraconazole maintenance therapy • Established (e.g., ≥6 months) adherence to effective cART • Negative <i>Histoplasma</i> blood cultures • Serum <i>Histoplasma</i> antigen <2 ng/mL <p>Use same initial itraconazole dosing for capsules as for solution. Itraconazole solution is preferred to the capsule formulation because it is better absorbed; solution can achieve serum concentrations 30% higher than those achieved with the capsules.</p>	November 6, 2013
Human Papillomavirus (HPV)	N/A	N/A	N/A	November 6, 2013
Influenza	N/A	N/A	No role for secondary chemoprophylaxis	July 17, 2018

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Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Isosporiasis (Cystoisosporiasis)	<p><u>If Severe</u> <u>Immunosuppression:</u></p> <ul style="list-style-type: none"> • TMP-SMX 2.5 mg/kg body weight of the TMP component (maximum 80 mg TMP) twice daily by mouth 3 times per week 	<p>Pyrimethamine 1 mg/kg body weight (maximum 25 mg) plus folinic acid, 5–15 mg by mouth once daily.</p> <p><u>Second-Line Alternative:</u></p> <ul style="list-style-type: none"> • Ciprofloxacin, 10–20 mg/kg body weight (maximum 500 mg) by mouth 3 times per week 	<p>Consider discontinuing secondary prophylaxis in patients without evidence of active <i>Isospora</i> infection who have sustained improvement in immunologic status (from CDC immunologic category 3 to CD4 values that fall within category 1 or 2) for >6 months in response to ART.</p> <p>In adults, the dose of pyrimethamine for secondary prophylaxis (25 mg daily) is lower than the dose for treatment (50–75 mg daily), but no data exist for dosing in children. Thus, the recommended dose for secondary prophylaxis in children is pyrimethamine 1 mg/kg (maximum 25 mg) by mouth once daily.</p> <p>Ciprofloxacin is not a drug of choice in children because of increased incidence of adverse events, including events related to joints and/or surrounding tissues.</p>	February 8, 2019
Malaria	<p><u>For <i>P. vivax</i> or <i>P. ovale</i>:</u></p> <ul style="list-style-type: none"> • Primaquine 0.5 mg/kg base (0.8 mg/kg salt) up to adult dose orally, daily for 14 days after departure from the malarious area 	N/A	<p>This regimen, known as PART, is recommended only for individuals who have resided in a malaria-endemic area for an extended period of time. Adult dose: 30 mg base (52.6 mg salt) orally, daily for 14 days after departure from the malarious area.</p> <p>http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/malaria.htm#1939</p>	November 6, 2013
Microsporidiosis	<p><u>Disseminated, Non-Ocular Infection or GI Infection Caused by Microsporidia Other Than <i>E. Bieneusi</i> or <i>V. Corneae</i>:</u></p> <ul style="list-style-type: none"> • Albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily <p><u>Ocular Infection:</u></p> <ul style="list-style-type: none"> • Topical fumagillin bicyclohexylammonium (Fumidil B) 3 mg/mL in saline (fumagillin 70 µg/mL) eye drops: 2 drops every 2 hours for 4 days, then 2 drops QID (investigational use only in United States) plus, for infection attributed to microsporidia other than <i>E. bieneusi</i> or <i>V. corneae</i>, albendazole 7.5 mg/kg body weight (maximum 400 mg/dose) by mouth twice daily for management of systemic infection 	N/A	<p><u>Criteria For Discontinuing Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> • After initiation of ART, resolution of signs and symptoms and sustained immune reconstitution (more than 6 months at CDC immunologic category 1 or 2) 	December 15, 2016

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Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
<i>Mycobacterium avium</i> Complex (MAC) (Chronic Suppressive Therapy)	<ul style="list-style-type: none"> • Clarithromycin 7.5 mg/kg body weight (maximum 500 mg) orally twice daily, plus • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g) orally once daily, with or without food • Children aged >5 years who received rifabutin as part of initial treatment: Rifabutin 5 mg/kg body weight (maximum 300 mg) orally once daily with food 	<ul style="list-style-type: none"> • Azithromycin 5 mg/kg body weight (maximum 250 mg) orally once daily, plus • Ethambutol 15–25 mg/kg body weight (maximum 2.5 g) orally once daily, with or without food • Children aged >5 years who received rifabutin as part of initial treatment: Rifabutin 5 mg/kg body weight (maximum 300 mg) orally once daily with food 	<p><u>Secondary Prophylaxis Indicated:</u></p> <ul style="list-style-type: none"> • Prior disease <p><u>Criteria for Discontinuing Secondary Prophylaxis</u></p> <p><i>Fulfillment of All of the Following Criteria:</i></p> <ul style="list-style-type: none"> • Completed ≥6 months of ART • Completed ≥12 months MAC therapy • Asymptomatic for signs and symptoms of MAC • Aged 2 to <6 years: CD4 count >200 cells/mm³ for ≥6 consecutive months • Aged ≥6 years: CD4 count >100 cells/mm³ for ≥6 consecutive months <p><u>Criteria for Restarting Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> • Aged 2 to <6 years: CD4 count <200 cells/mm³ • Aged ≥6 years: CD4 count <100 cells/mm³ 	January 8, 2019
<i>Mycobacterium Tuberculosis</i>	N/A	N/A	N/A	November 6, 2013
<i>Pneumocystis Pneumonia</i>	<ul style="list-style-type: none"> • TMP-SMX (Cotrimoxazole): TMP 2.5–5 mg/kg body weight/dose with SMX 12.5–25 mg/kg body weight/dose twice per day. Dosing based on TMP component. • The total daily dose should not exceed 320 mg TMP and 1600 mg SMX. Several dosing schemes have been used successfully— <ul style="list-style-type: none"> • Given 3 days per week on consecutive days or on alternate days • Given 2 days per week on consecutive days or on alternate days <ul style="list-style-type: none"> • Given every day (total daily dose of TMP 5–10 mg/kg body weight given as a single dose each day) 	<p><u>Dapsone</u></p> <p><i>Children aged ≥1 months:</i></p> <ul style="list-style-type: none"> • 2 mg/kg body weight (maximum 100 mg) by mouth once daily or 4 mg/kg body weight (maximum 200 mg) by mouth once weekly <p><u>Atovaquone</u></p> <p><i>Children Aged 1–3 Months and >24 Months–12 Years:</i></p> <ul style="list-style-type: none"> • 30–40 mg/kg body weight/dose by mouth once daily with food <p><i>Children Aged 4–24 Months:</i></p> <ul style="list-style-type: none"> • 45 mg/kg body weight/dose by mouth once daily with food <p><i>Children Aged ≥13 Years:</i></p> <ul style="list-style-type: none"> • 1500 mg (10 cc oral yellow suspension) per dose by mouth once daily <p><u>Aerosolized Pentamidine</u></p> <p><i>Children Aged ≥5 Years:</i></p> <ul style="list-style-type: none"> • 300 mg every month via Respigard II™ nebulizer (manufactured by Marquest; Englewood, Colorado) 	<p><u>Secondary Prophylaxis Indicated For:</u></p> <ul style="list-style-type: none"> • Children with prior episode of PCP <p><u>Criteria for Discontinuing Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> • Same as for primary prophylaxis <p><u>Criteria for Restarting Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> • Same as for primary prophylaxis 	November 6, 2013

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Indication	First Choice	Alternative	Comments/Special Issues	Last Reviewed
Syphilis	N/A	N/A	<p><u>Secondary Prophylaxis Indicated:</u></p> <ul style="list-style-type: none"> N/A <p><u>Criteria For Discontinuing Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> N/A <p><u>Criteria For Restarting Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> N/A 	November 6, 2013
Toxoplasmosis (Suppressive Therapy)	<ul style="list-style-type: none"> Sulfadiazine 42.5–60 mg/kg body weight per dose twice daily* (maximum 2–4 g per day) by mouth, plus Pyrimethamine 1 mg/kg body weight or 15 mg/m² body surface area (maximum 25 mg) by mouth once daily, plus Leucovorin 5 mg by mouth once every 3 days 	<ul style="list-style-type: none"> Clindamycin 7–10 mg/kg body weight per dose by mouth 3 times daily, plus Pyrimethamine 1 mg/kg body weight or 15 mg/m² body surface area (maximum 25 mg) by mouth once daily, plus Leucovorin 5 mg by mouth once every 3 days <p><u>Children Aged 1–3 Months and >24 Months:</u></p> <ul style="list-style-type: none"> Atovaquone 30 mg/kg body weight by mouth once daily Leucovorin, 5 mg by mouth every 3 days TMP-SMX, 150/750 mg/m² body surface area once daily by mouth <p><u>Children Aged 4–24 Months:</u></p> <ul style="list-style-type: none"> Atovaquone 45 mg/kg body weight by mouth once daily, with or without pyrimethamine 1 mg/kg body weight or 15 mg/m² body surface area (maximum 25 mg) by mouth once daily, plus Leucovorin, 5 mg by mouth every 3 days TMP-SMX, 150/750 mg/m² body surface area once daily by mouth 	<p><u>Secondary Prophylaxis Indicated:</u></p> <ul style="list-style-type: none"> Prior toxoplasmic encephalitis <p>Note: Alternate regimens with very limited data in children. TMP-SMX only to be used if patient intolerant to other regimens</p> <p><u>Criteria for Discontinuing Secondary Prophylaxis</u></p> <p><i>If All of the Following Criteria are Fulfilled:</i></p> <ul style="list-style-type: none"> Completed ≥6 months of cART, completed initial therapy for TE, asymptomatic for TE, and Aged 1 to < 6 years; CD4 percentage ≥15% for >6 consecutive months Aged ≥6 years; CD4 cell count >200 cells/mm³ for >6 consecutive months <p><u>Criteria For Restarting Secondary Prophylaxis:</u></p> <ul style="list-style-type: none"> Aged 1 to <6 years with CD4 percentage <15% Aged ≥6 years with CD4 cell count <200 cells/mm³ 	November 6, 2013
Varicella-Zoster Virus (VZV)	N/A	N/A	There is no indication for secondary prophylaxis	December 9, 2019

Key to Acronyms: BID = twice daily; BSA = body surface area; cART = combination antiretroviral therapy; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; CNS = central nervous system; CrCl = (estimated) creatinine clearance; CSF = cerebrospinal fluid; GI = gastrointestinal; HBV = hepatitis B virus; HCV = hepatitis C virus; HSV = herpes simplex virus; IV = intravenous; IVIG = intravenous immunoglobulin; MAC = mycobacterium avium complex; PCP = pneumocystis pneumonia; QID = 4 times a day; SQ = subcutaneous; TE = toxoplasmic encephalitis; TID = three times daily; TMP-SMX = trimethoprim-sulfamethoxazole